

- a) H-,
- b) (C₁-C₄)alkyl,
- c) aryl(CH₂)_m,
- d) ClH₂C-,
- e) Cl₂HC-,
- f) FH₂C-,
- g) F₂HC-, and
- h) (C₃-C₆)cycloalkyl;

R¹⁹ is selected from the group consisting of:

- a) CH₃,
- b) CH₂Cl,
- c) CH₂CH=CH₂,
- d) aryl, and
- e) CH₂CN;

R²⁰ is OH, CH₃O-, or F;

R²¹ is:

- a) CH₃-,
- b) HOCH₂-,
- c) aniline, or
- d) (CH₃)₂N-CH₂-,

R²² is selected from the group consisting of:

- a) HO-
- b) CH₃O-
- c) H₂N-
- d) CH₃OC(O)O-,
- e) CH₃C(O)OCH₂C(O)O-,
- f) aryl-CH₂OCH₂C(O)O-,
- g) HO(CH₂)₂O-,
- h) CH₃OCH₂O(CH₂)₂O-, and
- i) CH₃OCH₂O-;

m is 0 or 1;

n is 1-3;

p is 0-2; and

aryl is unsubstituted phenyl or phenyl unsubstituted with one of the following:

- a) F,
- 5 b) Cl,
- c) OCH₃,
- d) OH,
- e) NH₂,
- f) (C₁-C₄)alkyl,
- 10 g) OC(O)OCH₃, or
- h) NO₂;

and protected forms thereof.

Specific substituted Q¹ groups include, but are not limited to, 4-(benzyloxycarbonyl)-1-piperazinyl, 4-morpholinyl, and 4-hydroxyacetyl piperazinyl.

- 15 Especially preferred R¹ groups include 3-fluoro-4-[4-(benzyloxycarbonyl)-1-piperazinyl]phenyl, 3-fluoro-4-(4-morpholinyl)phenyl, 4-(1,1-dioxohexahydro-1λ⁶-thiopyran-4-yl)-3-fluorophenyl, 3-fluoro-4-tetrahydro-2H-thiopyran-4-ylphenyl, 3,5-difluoro-4-(4-thiomorpholinyl)phenyl, 3-fluoro-4-(3-thietanyl)phenyl, and 4-(1,1-dioxido-3-thietanyl)-3-fluorophenyl.

- 20 R² is selected from the group consisting of C₁-C₂₀ alkyl, C₃-C₇ cycloalkyl, aryl optionally substituted with one or two C₁-C₃alkyl or halogen groups, allyl, 3-methylallyl, 3,3-dimethylallyl, vinyl, styrylmethyl, benzyl optionally substituted on the phenyl with one or two Cl, C₁-C₄ alkyl, nitro, cyano, or trifluoromethyl groups, 9-fluorenylmethyl, trichloromethylmethyl, 2-
- 25 trimethylsilylethyl, phenylethyl, 1-adamantyl, diphenylmethyl, 1,1-dimethylpropargyl, 2-furanylmethyl, isobornyl, and hydrogen. Preferably, R² is methyl. R³ is C₁-C₁₀ alkyl, and, preferably, R³ is C₄-C₇ tertiary alkyl.

- The carbamate (I) and S-epoxide (II) are reacted in the presence of a base and a solvent. The identity of the base is not critical as long as the base is
- 30 capable of deprotonating carbamate (I), i.e., a base whose conjugate acid has a pK_a of greater than about 8. A preferred base is selected from the group consisting of an

- alkoxy group having one through seven carbon atoms; a carbonate; a methyl, sec-butyl or t-butyl carbanion; tri(alkyl)amine, wherein the alkyl group contains 1 through 5 carbon atoms; a conjugate base of carbamate (II); 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU); 1,5-diazabicyclo[4.3.0]non-5-ene (DBN); N-methylpiperidine; N-methylmorpholine; and, 2,2,2-trichloroethoxide. The most preferred base is an alkoxy group having four or five carbon atoms, particularly t-amylate or t-butoxide. Sodium or potassium bases in combination with a lithium salt (such as, lithium chloride or lithium bromide) can be used to form the lithium cation and base *in situ*.

- The identity of the solvent also is not critical, and includes, for example, cyclic ethers such as tetrahydrofuran (THF), amides such as dimethylformamide (DMF) and dimethylacetamide (DMAC), amines such as triethylamine, acetonitrile, and alcohols such as t-amyl alcohol and t-butyl alcohol. The choice of solvent is related to the solubility of carbamate (I) and the S-epoxide (II), and can be determined easily by those skilled in the art.

- Another embodiment of the present invention is set forth in Scheme 2,

Scheme 2

